FOURTEENTH INTERNATIONAL

# ROTAVIRUS SYMPOSIUM

MARCH 14–16 **2023** BALI INDONESIA

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# EFFECTIVENESS EVALUATION OF ROTAVIRUS VACCINE IN VIETNAM

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Rotavin VE team

# ACKNOWLEDGEMENTS


- Funding Source:
  - Bill and Melinda Gates Foundation via CDC Foundation
  - POLYVAC, Vietnam
- Technical advices:
  - US Centers for Disease Control and Prevention
  - National Expanded Immunization Program
  - Expanded Program for Immunization - Northern Vietnam

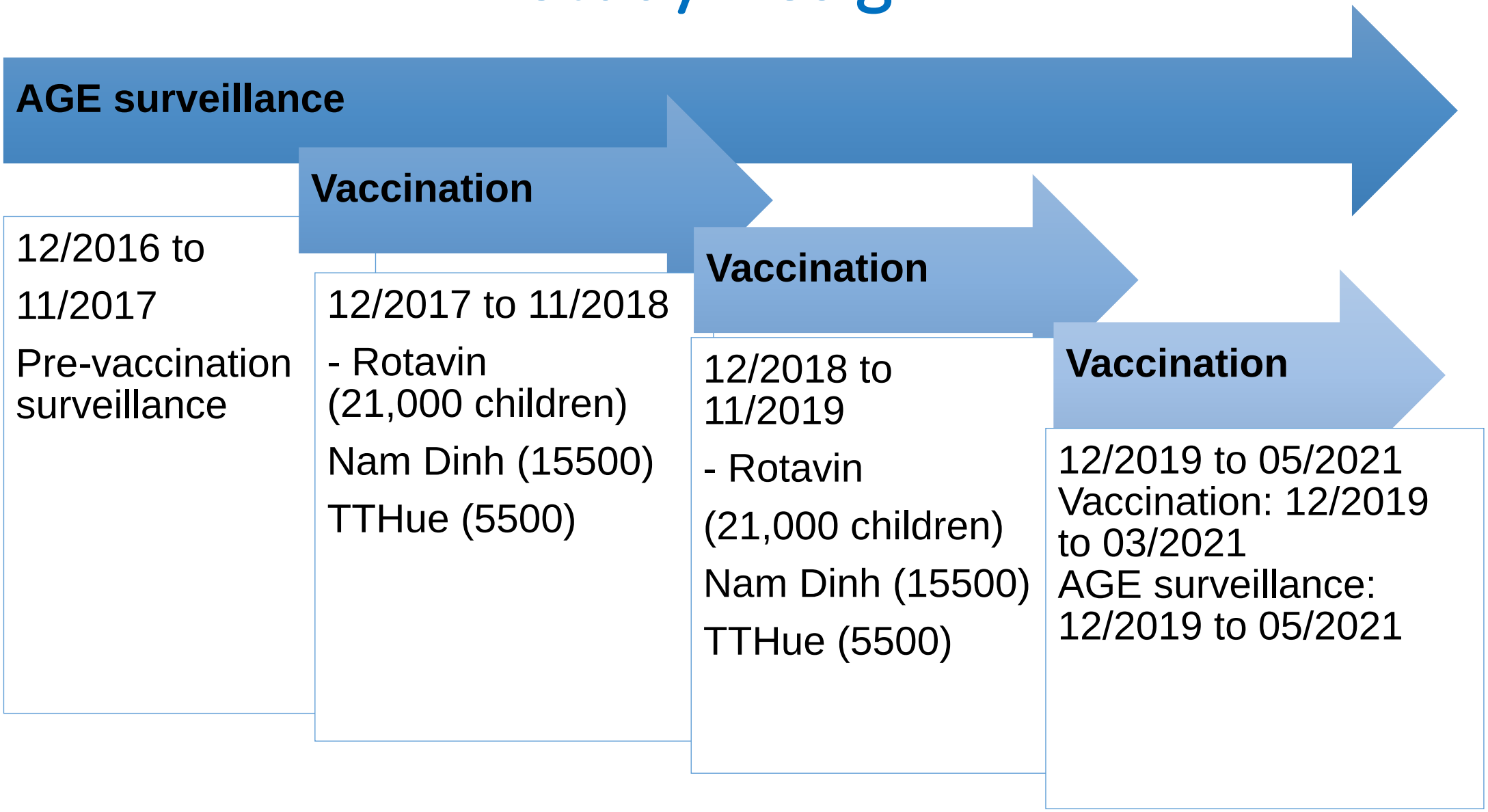
# Current situation of rotavirus vaccines in Vietnam

- Surveillance in Vietnam show high burden of rotavirus related diarrhea among hospitalized children, ˜50% (1998-2010),˜ 40% (2011-2018) (Van man 2005, Ander 2015, Huyen 2018)
- Rotavin-M1 (G1P[8]) was developed by POLYVAC-USCDC from a strain isolated from fecal sample of a patient (2003). The vaccine (-20$^{o}$C formula) underwent phase 1, 2 and 2+ clinical trials, approved in 2012 and has been used in private markets since then (2.6 million doses)
- Rotavin (2-8$^{o}$C) (POLYVAC-PATH): non-inferiority study with Rotavin (-20$^{o}$C) (Thiem et al 2021), approved in Jan 2022
- Other rotavirus vaccines are available in Vietnam
  - Rotateq, Vaccine efficacy : 63% (Zahman, Anh DD 2010)
  - Rotarix, VE: 70% (DungThi, 2021)
  - Rotavac: safety/immunogenicity only (Hai, 2021)

# Objectives

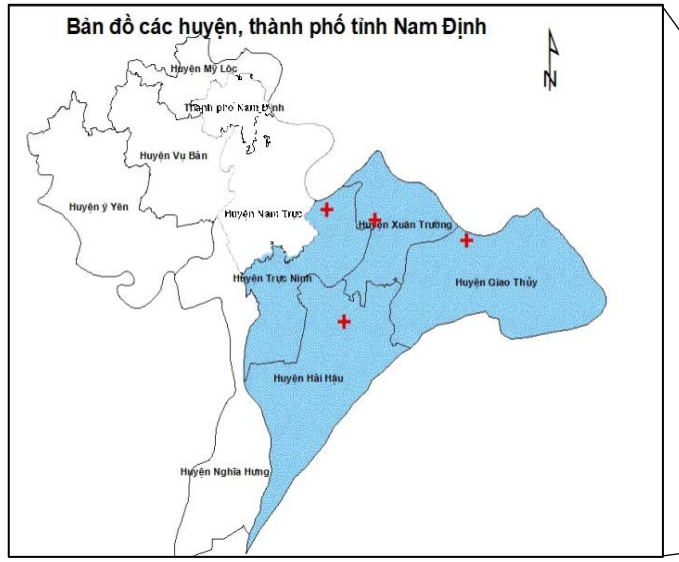
- Impact of Rotavin-M1 to diarrheal diseases (all causes and RV – related) when introduced together with other EPI vaccines
- Effectiveness of Rotavin-M1 against RV related diarrhea

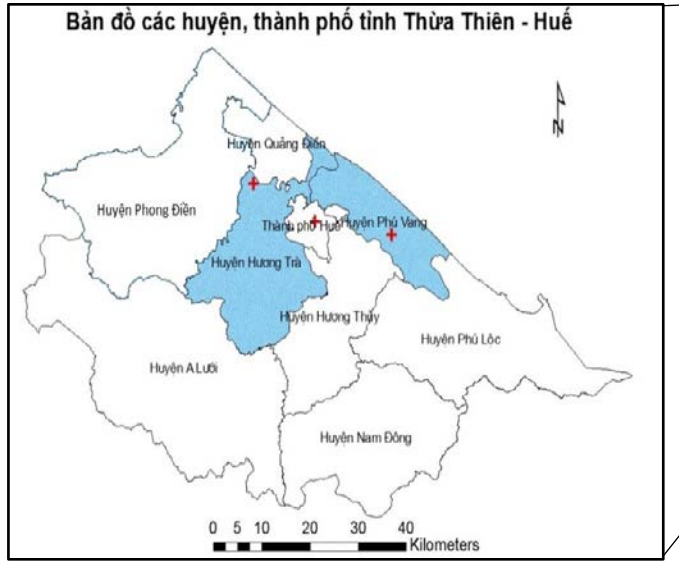
# Study Design

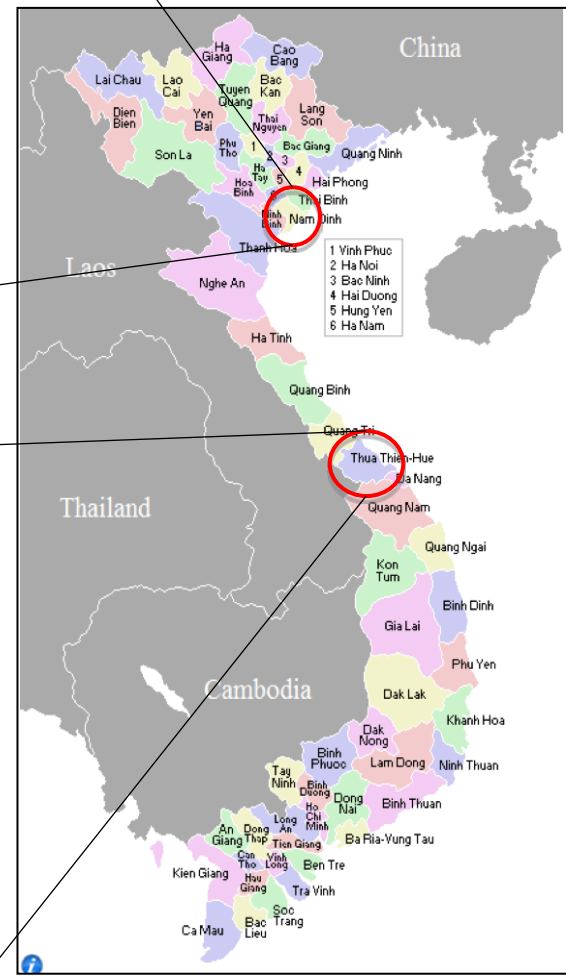


# Study sites

- Nam Dinh:
  - located in the North
  - 4 districts (out of 10) in Nam Định *(birth co-hort 15500/year)*
  - Hai Hau, Giao Thuy, Xuan Truong, and Truc Ninh hospitals, 98 commune health center
  - Distinct seasonal peaks – October-March
- T.T Hue:
  - located in the central region of Vietnam
  - 2 districts (out of 9) in T.T Hue *(birth co-hort 5500/year)*
  - Huong Tra, Phu Vang (2016-2021), and Hue Center (2016-2018) hospitals
  - 36 commune health centers
  - Less distinct seasonal peaks – January-June





# Diarrheal surveillance

- Enroll all AGE cases of children less than 5 years hospitalized in 6 district hospitals and 1 central hospital

- Collect fecal samples and epi/clinical/vaccination information
  - EPI database
  - Vaccination record books at commune health centers
  - Personal vaccination cards

# RESULTS

# Rotavin vaccination – 12/2017- 12/ 2021

During 3 years of vaccine introduction in Nam Dinh and Hue (12/2017-12/2020),

- Nam Dinh: 38,421 children received 1st dose, 36,964 received 2nd dose
- Hue: 14,473 children received 1st dose, 13,485 received 2nd dose

# Diarrheal case enrollment – December 2016-May 2021

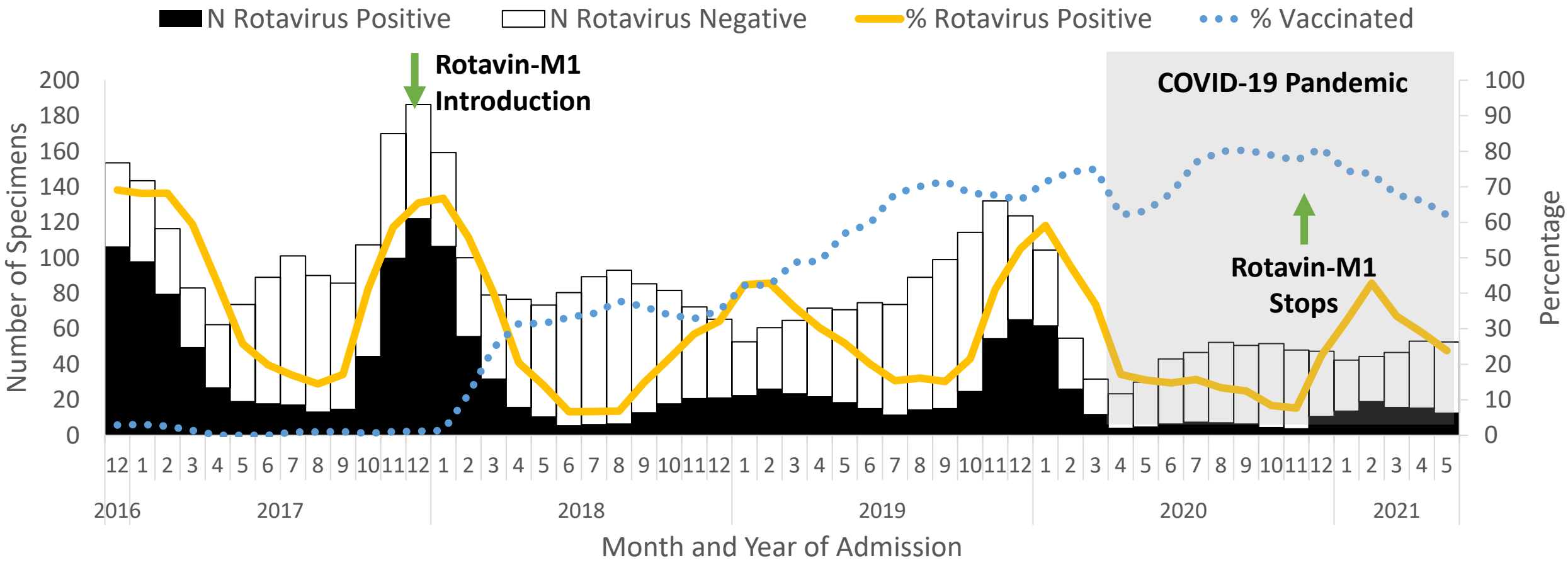
| | Nam Dinh | TT Hue | Total |
|---|---|---|---|
| **Enrolled children** | 4,662 | 2,566 | 7,228 |
| **Stool specimen collected** | 4,428 (95%) | 2,349 (92%) | 6,777 (94%) |
| **Specimens tested by ELISA** | 4,366 (99%) | 2,260 (96%) | 6,626 (98%) |
| **Rotavirus positive** | 1,553 (35%) | 611 (26%) | 2,164 (32%) |
| **Age-eligible to receive rotavirus vaccine*** | 1,377 | 489 | 1,866 |
| **Received at least one dose of Rotavin-M1** | 1,066 (77%) | 203 (42%) | 1,269 (68%) |

*Restricted to children that were hospitalized for non-rotavirus diarrhea and had a verified vaccination status

# RESULTS

Objective #1: Impact of Rotavin-M1 to diarrheal diseases (all causes and RV – related) when introduced together with other EPI vaccines

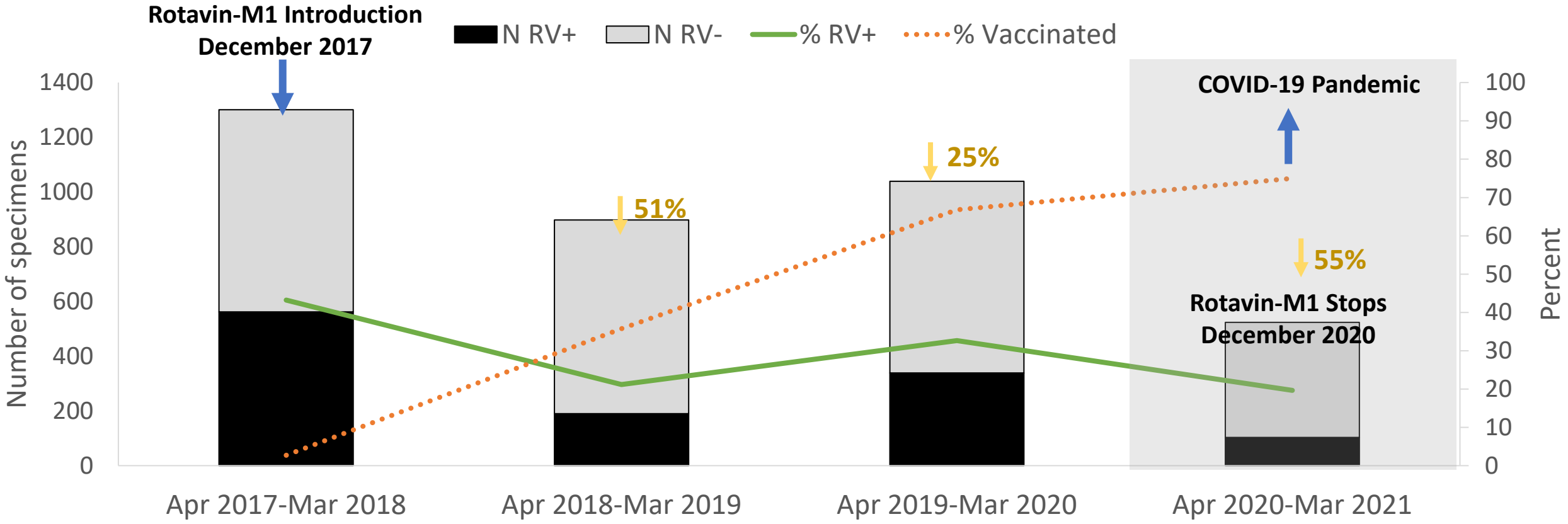
# Rotavirus Detection by Month in Nam Dinh Province among Children <5 Years of Age, Dec 2016 - May 2021




Peaks were blunted, with biennual pattern following vaccine introduction

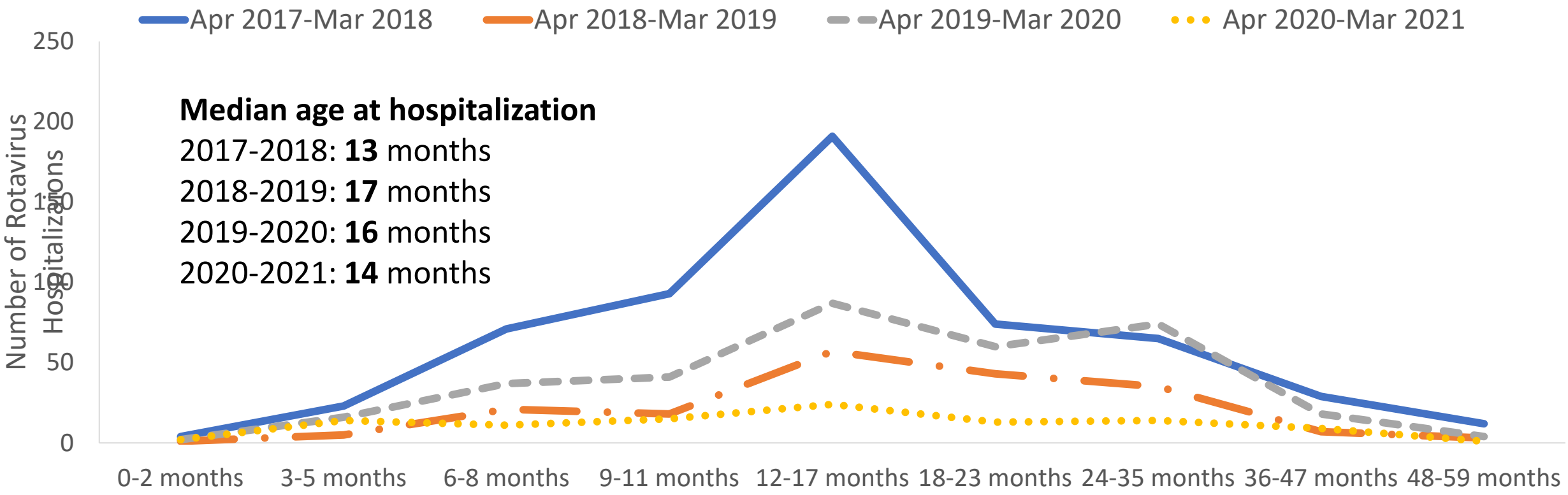
*3 month moving average

# Rotavirus Detection and Rotavirus Vaccine Coverage by Season in Nam Dinh Province among Children <5 Years of Age, April 2017 - March 2021



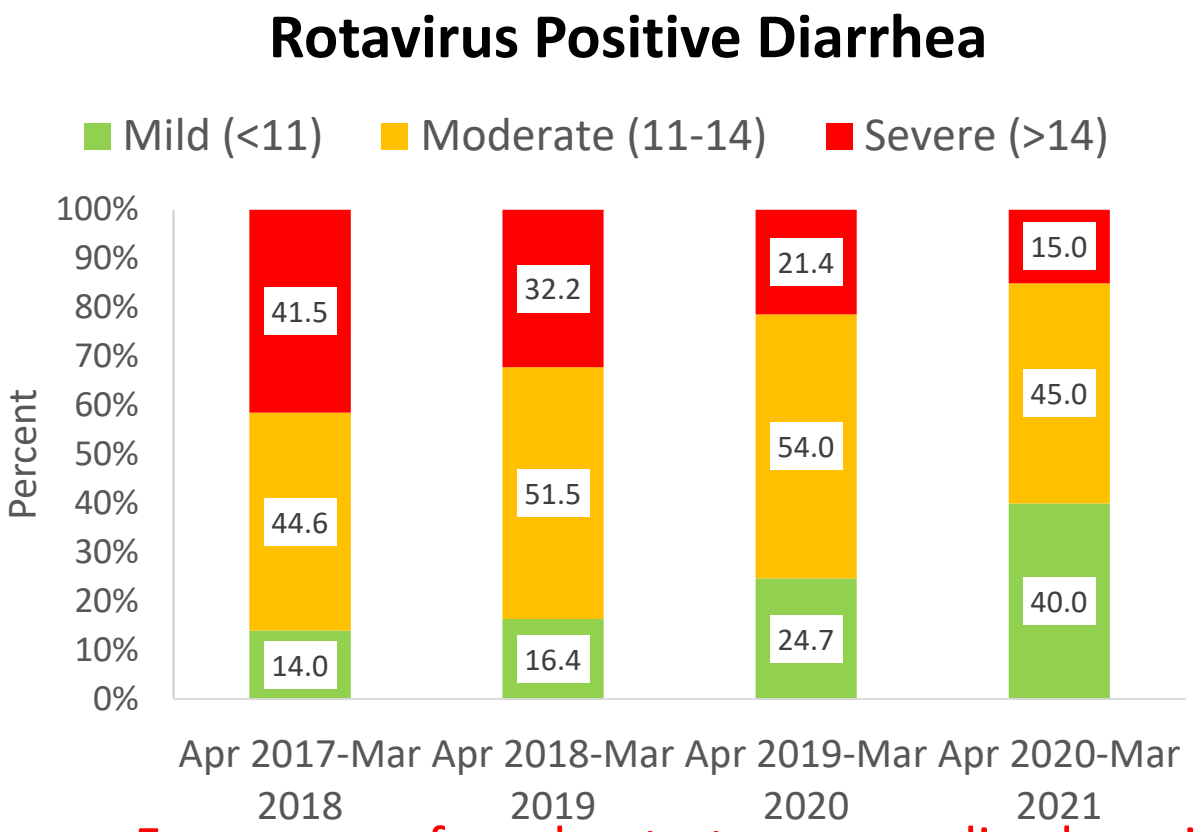

- Rotavirus positivity significantly decline by 51% in the first year, 25% in the 2nd year and 55% in the 3rd year of vaccine introduction. Overall reduction rate: 40.6%.
- Coverage  with at least 1 dose increased from 35.7% in the first year to 75% in the 3rd year

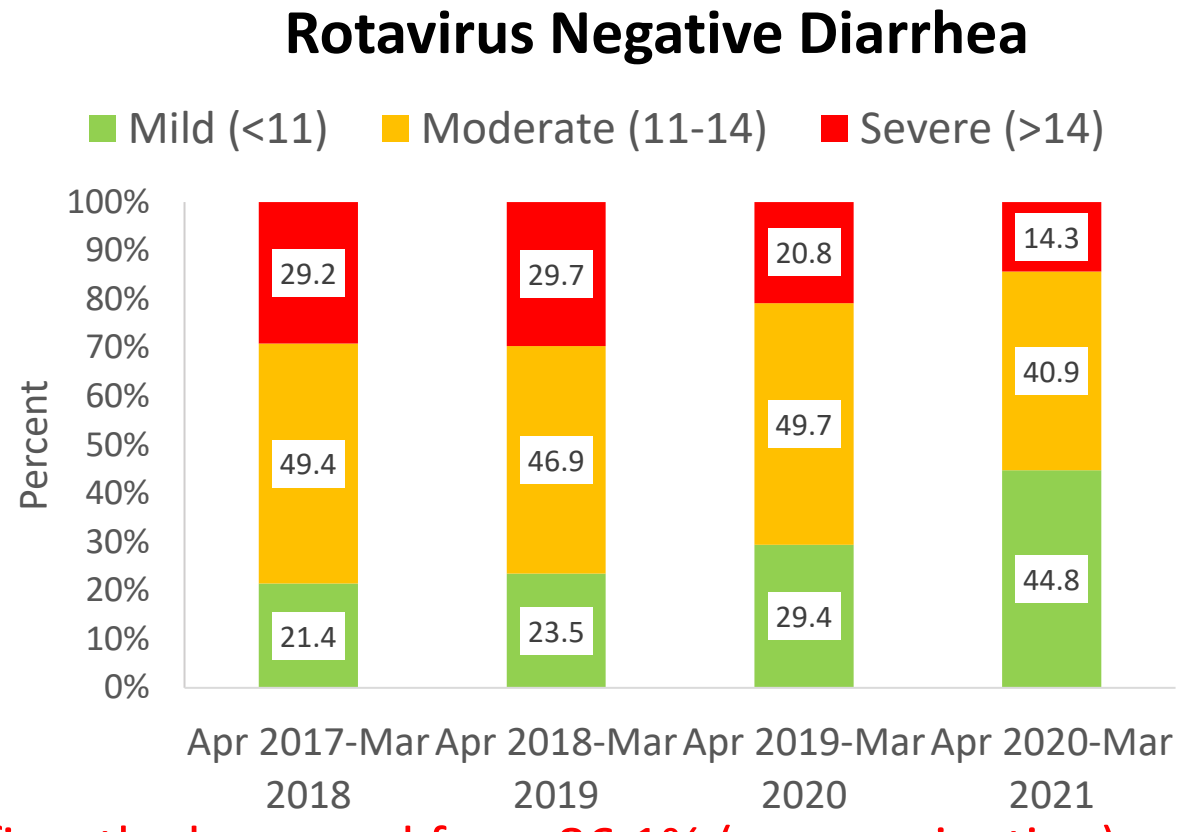
# Number of Rotavirus Positive Hospitalizations by Age Group and Year, Nam Dinh Province, April 2017-March 2021




- Before vaccine introduction, rotavirus hospitalization peaked in children 12-17 months of age, the peak was less pronounce post introduction.
- Mean age of hospitalization increased post vaccine introduction

# Severity Distribution of Diarrhea Hospitalizations by Rotavirus Season among Children <5 Years of Age, Nam Dinh Province, April 2017-March 2021




- Frequency of moderate-to-severe diarrhea significantly decreased from 86.1% (pre-vaccination) to 83.7, 75.4, 60% in 1st, 2nd, and 3rd year (post vaccination) among RV positive diarrhea.
- Higher overall severity among RV positive compared with RV negative children

# Vaccine Effectiveness

**Objective#2**: To determine the effectiveness of a full course of Rotavin-M1 in preventing moderate-to-severe rotavirus disease under conditions of routine use

# Determining rotavirus vaccine effectiveness

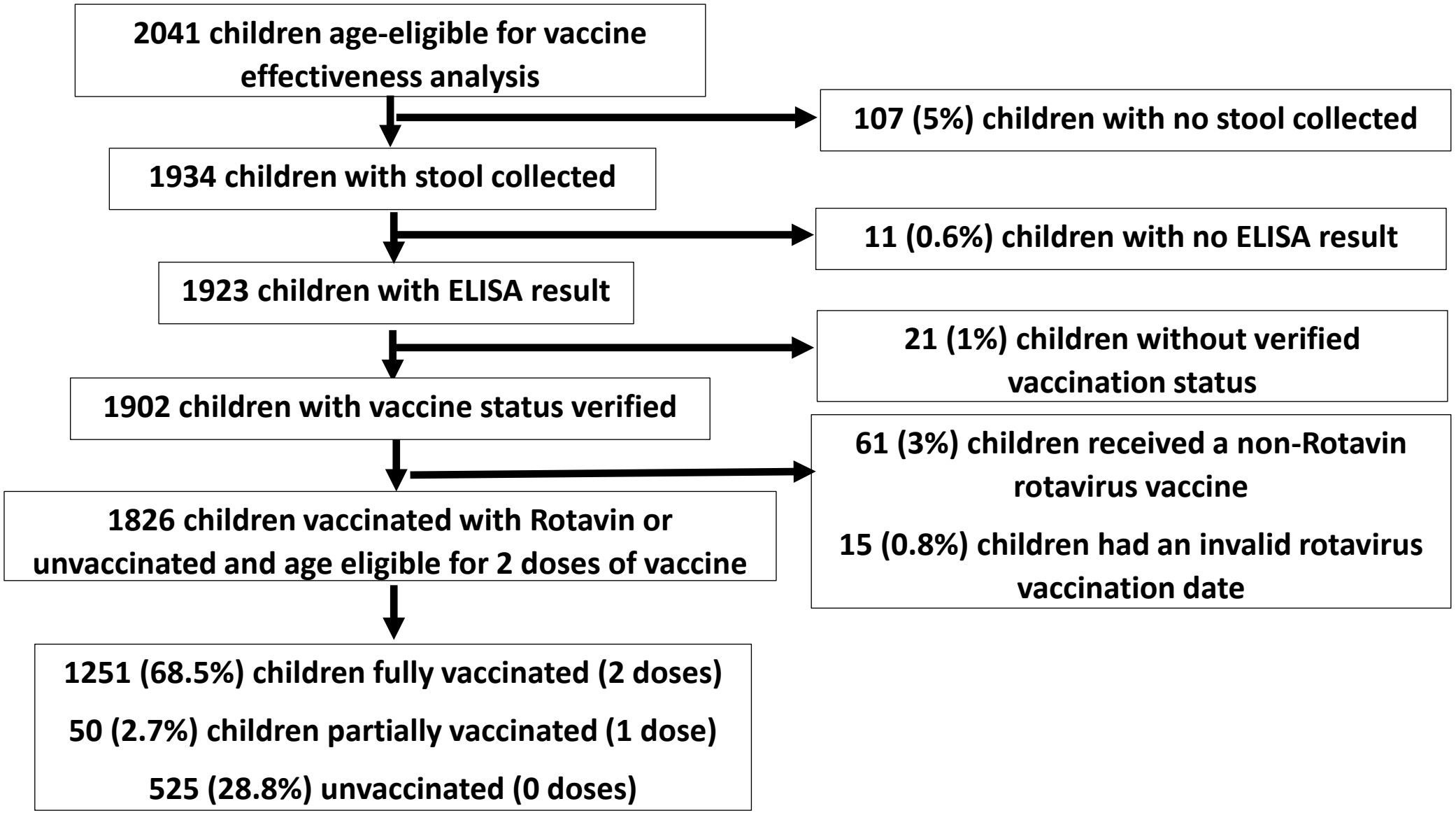
- Case-control evaluations built on active rotavirus surveillance platforms

- **Cases**: vaccine age-eligible children with acute diarrhea (≥3 loose stools in 24 hrs) who test **positive** for rotavirus by enzyme immunoassay (EIA)

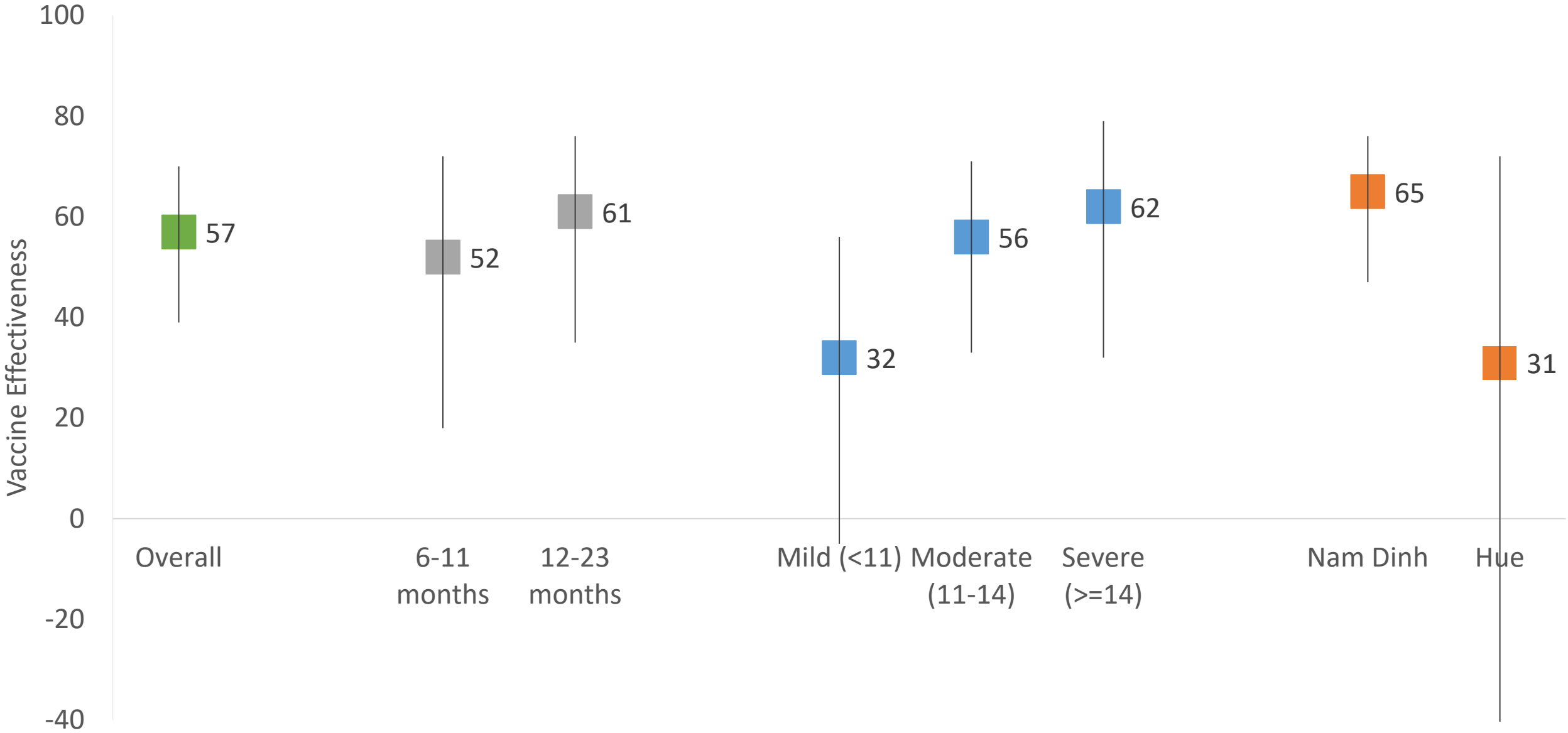
- **Test-negative controls**: vaccine age-eligible children with acute diarrhea (≥ 3 loose stools in 24 hrs) who test **negative** for rotavirus by EIA

- **Vaccination status** confirmed by electronic clinic registry or vaccine card

# Enrollment for Vaccine Effectiveness Evaluation

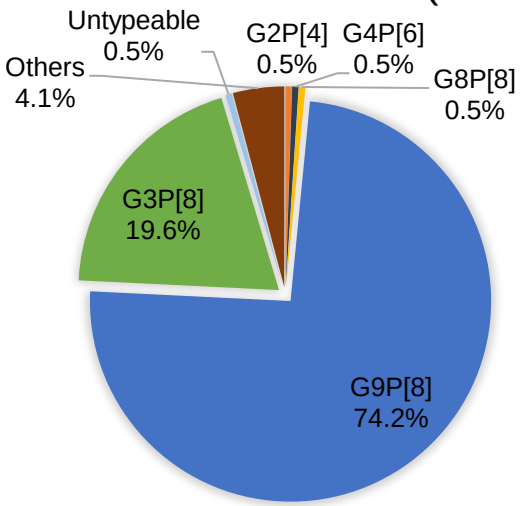


# Effectiveness of Rotavin-M1

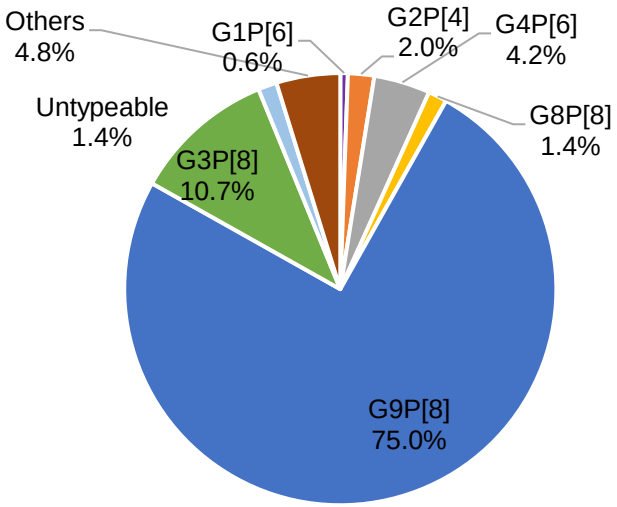


# Prevalence of RVA G/P genotype in Nam Dinh

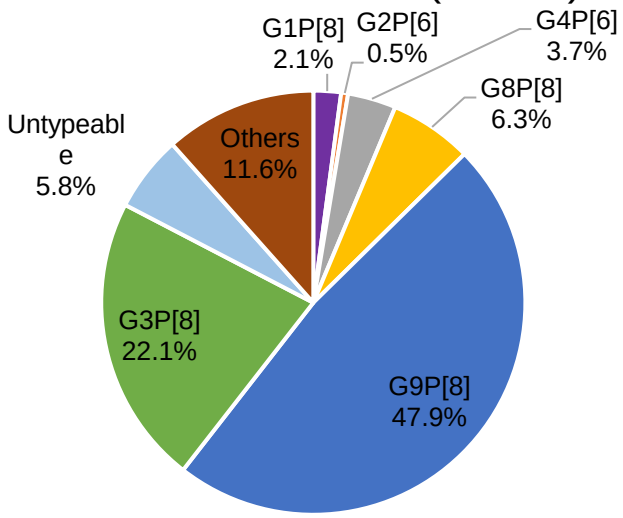
BEFORE 04/2017 (N=194)



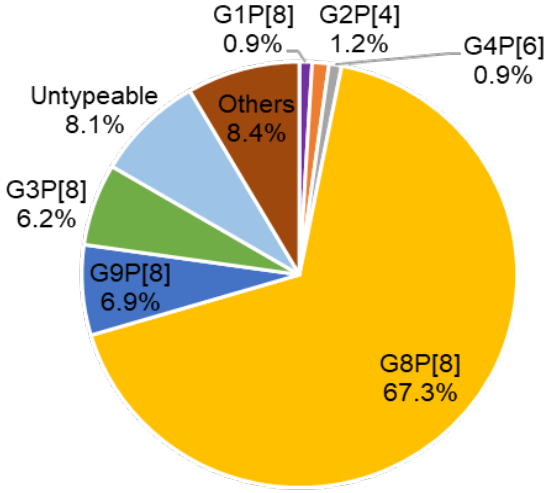

04/2017-03/2018 (N=356)



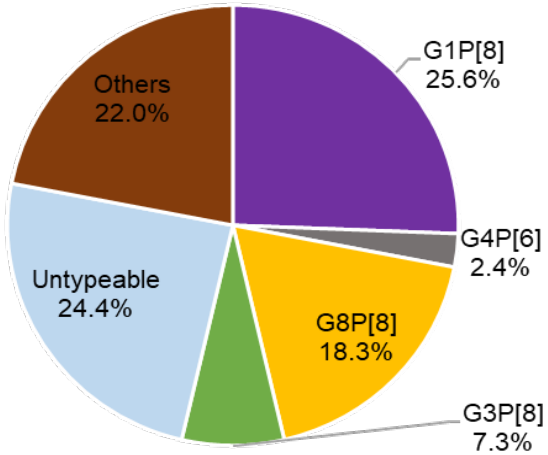

04/2018-03/2019 (N=190)




04/2019-03/2020 (N=321)




04/2020-03/2021 (N=82)



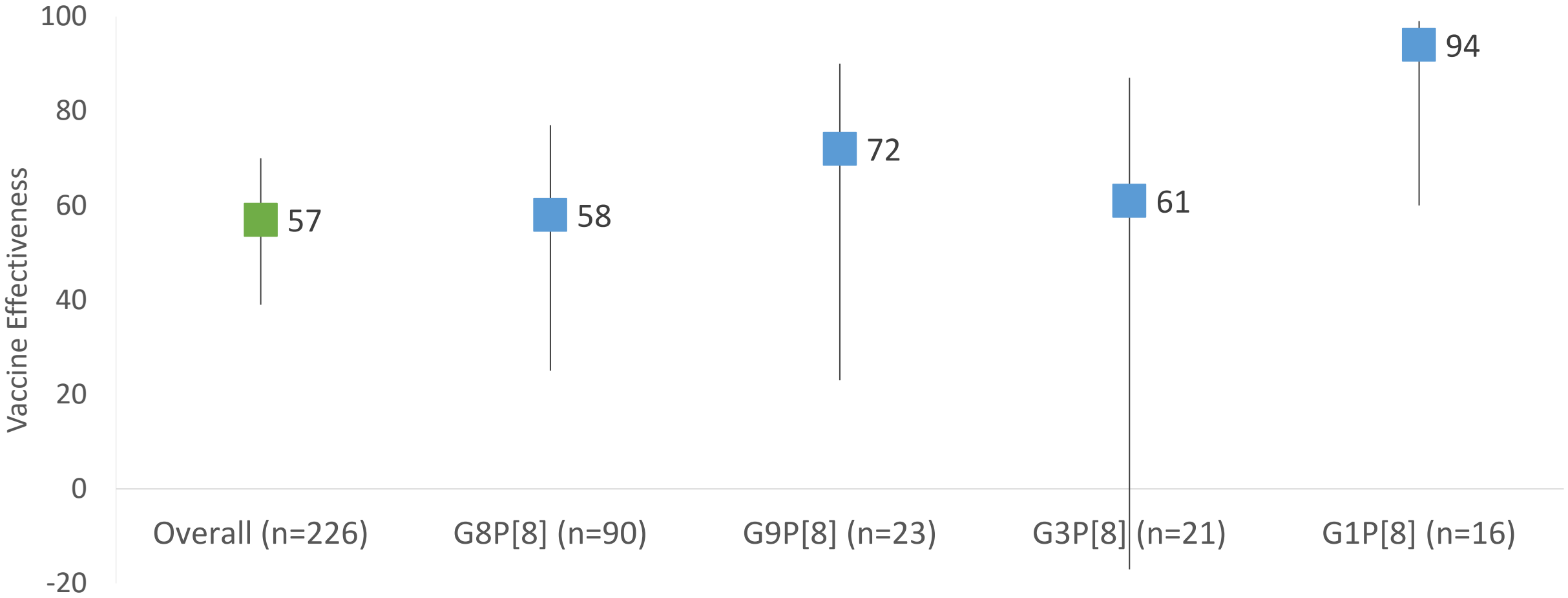

Pre-vaccine introduction, G9P[8] is predominant type

1st year: G9P[8], G3P[8]

2nd year: G8P[8]

3rd year: G1P[8], G8P[8]

# Vaccine Effectiveness by Genotype




Among age-eligible 6-23 months of age children, Full 2 doses Rotavin-M1 was 57% effective against hospitalization for moderate to severe RV diarrhea

# Summary

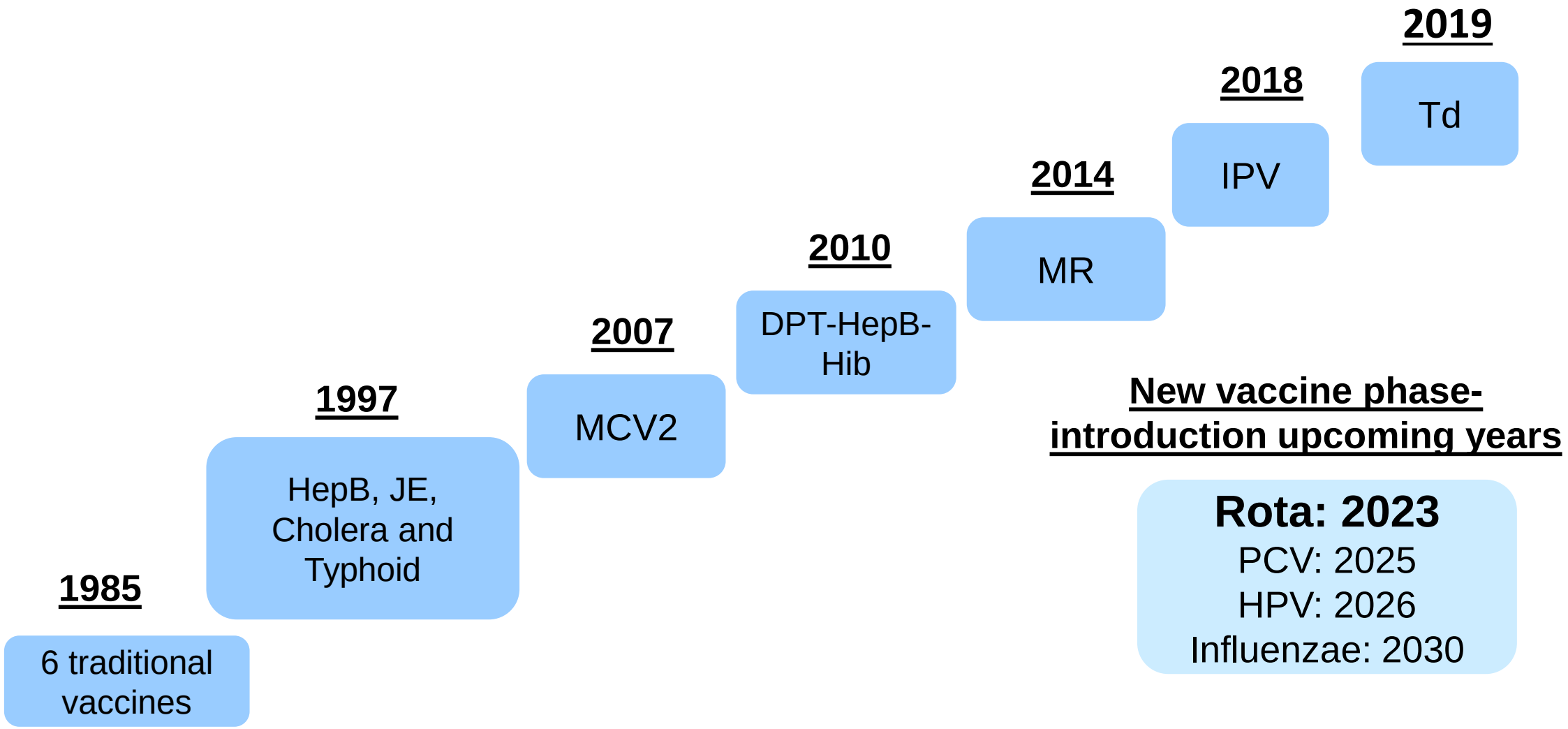
- Rotavirus hospitalizations declined in **Nam Dinh** following vaccine introduction
  - Vaccine coverage peaked at 70-75% during third post-vaccine introduction year
  - Sharp seasonal peaks blunted
  - Biennial pattern appeared emerge with slight increase in disease during the second post-vaccine introduction year but remained below pre-vaccine levels
    - Likely due to accumulation of susceptible children

# Summary

- Full 2-dose series of Rotavin-M1 **57% effective** against moderate-to-severe rotavirus disease in children 6-23 months of age
  - Protection extended through the second year of life
  - Effectiveness increased with increasing severity of disease
  - Protective against a range of circulating genotypes
  - Similar efficacy to RotaTeq from clinical trial (63%) and to a post-licensure study in private market Ho Chi Minh (70%) where most children received Rotarix

- **Conclusion:** Rollout of the vaccine at the national level with efforts to achieve high coverage in all districts may have substantial impact on rotavirus disease burden in Vietnam

# Vaccine introduction into EPI




Courtesy from Dang Thanh Huyen et al, 2023

# THANK YOU FOR YOUR ATTENTION